

**Saskatchewan**

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**FINAL REPORT**

**UNDERSTANDING THE EPIDEMIOLOGY OF PORCINE  
CIRCOVIRUS**

**19970099**

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**Prepared by: Harding Swine Vet Services Inc.**



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**Final Report****UNDERSTANDING THE EPIDEMIOLOGY OF PORCINE CIRCOVIRUS****Principle Investigator:****Dr. John Harding****Co-investigators:****Dr. John Ellis****Dr. Charles Rhodes****Dr. Hugh Townsend****SUMMARY**

Post-weaning Multisystemic Wasting Syndrome (PMWS) is a new emerging disease of swine, originally reported in a single Saskatchewan herd in 1995. PMWS can cause severe disease in weaned pigs resulting in a 3-4 fold increase in mortality, but more commonly is an insidious disease. PMWS is thought to be caused by porcine circovirus type 2 (PCV-2), which is genetically distinct from the non-pathogenic subtype, PCV-1. The objective of this study was to investigate the epidemiology of PCV-2 in terms of antibody development, in closely related swine farms. A further objective was to determine if differences in the antibody level exist or are associated with productivity within herds of a large breeding stock system. Herds experiencing PMWS suffered higher post-weaning mortality and clinical signs of unthriftiness, jaundice and pallor. However, PCV-2 antibody levels were similar in herds experiencing clinical disease compared to those that were not. All herds demonstrated high levels of PCV-2 antibodies, and 98.8% of all finisher animals were positive for antibody. It is concluded that PCV-2 infection is wide spread within the herds studied, but is not solely responsible for the development of clinical disease.



## **B) TECHNICAL REPORTS**

### **Introduction**

Since its discovery in 1995, the distribution and prevalence of post-weaning multisystemic wasting syndrome (PMWS) has increased worldwide. In Canada, it has been diagnosed in all provinces from Quebec through Alberta, although it is clearly more prevalent in the prairies. In the USA it has been diagnosed in numerous states and continues to be of great interest in the peer reviewed scientific press, scientific meetings and the lay media. In 1999, it was identified as a research priority by National Pork Producer's Health Summit and was included in a December 1999 workshop studying the response of Canadian Food Inspection Agency's to emerging disease threats in Canada. Currently there is very strong, if not conclusive evidence suggesting that porcine circovirus type 2 (PCV-2) is the cause of PMWS, however additional viral and/or bacterial pathogens are necessary to exacerbate the clinical disease.

PCV-1 was first identified as non-cytopathic contaminant of the PK15 cell line, and is largely accepted as being nonpathogenic to swine (Tischer et al, 1986, Tischer et al, 1974). In 1998, a genetically distinct variant strain of PCV-2, has been isolated from pigs with PMWS (Ellis et al, 1998).

Serum antibodies to PCV-1 are wide spread in the swine industries of Germany (Tischer 1995), Canada (DuLac 1989), England (Edwards 1994), and the USA (Hines, 1995). A competitive ELISA test for the detection of PCV-2 antibody was recently been developed by Dr. John Ellis and coworkers at the Western College of Veterinary Medicine. Unlike other tests measuring serum antibodies to porcine circovirus, the competitive ELISA is specific for type 2 PCV, and minimizes cross reactions with PCV-1. The competitive ELISA is adapted to mass screening, is less subjective and facilitates superb titration of titre level. Thus, it is well suited for serologic profiling by age group and is an excellent tool for facilitating a better understanding of the epidemiology of PMWS.

The clinical presentation and pathology of PMWS have been previously described (Harding et al, 1998, Harding & Clark, 1998, Harding 1996) and is beyond the scope of this report. However, a recent manuscript is attached to this report which further describes the clinical presentation of PMWS.

### **Project Objectives**

The project objectives as originally described in the grant application of June 1997 are as follows:

- 1) perform a pilot epidemiologic study of porcine circovirus infection in representative swine herds,
- 2) propose potential control strategies in infected farms with and without clinical disease,
- 3) identify further areas of epidemiologic research necessary in order to develop more comprehensive control strategies.

### **Project Activities**

Two experiments were undertaken. Experiment 1 was undertaken to determine the pattern of PCV-2 serum antibody development and decay in farrow to finish herds. Knowledge of this was critical to the design of experiment 2. Experiment 2 was a case-control study, characterizing the PCV-2 antibody response in herds experiencing PMWS (clinical) compared to similar herds that were not (non-clinical).

The results of this project have been presented at three veterinary science meetings. For each meeting, aspects of the project and results were reviewed, followed by a summary for the meeting proceedings.

- a) Allan D. Leman Swine conference - St Paul, MN, September 1999  
"The clinical expression of Porcine Circovirus"
- b) Western Canadian Association of Swine Practitioners - Saskatoon, SK, October 1999  
"Porcine circovirus-2: competitive ELISA titres of clinical and non-clinical herds"
- c) Italian Pig Veterinary Society Annual Meeting - Piacenza, Italy, March 2000  
"PMWS - clinical aspects, epidemiology and diagnosis"

### **Project Results**

The trial design, results and conclusions for each experiment are presented below.

## **Experiment 1:**

### **Analysis of PCV-2 antibody titres using the competitive ELISA in farrow to finish herds: a pilot study**

#### **Introduction**

The objectives of this experiment were to crudely characterize the pattern of PCV-2 antibody development and decay in farrow to finish herds using the competitive ELISA, specific for type 2 porcine circovirus. Past investigations of similar nature had used antibody tests developed for PCV-1 and failed to elucidate the prevalence of PCV-2 antibodies in the industry, or in affected farms. Results from this experiment used to determine the most cost effective sampling method for the case control study, experiment 2 of this project.

#### **Materials and Methods**

From a bank of frozen serum held by Harding Swine Vet Service Inc., 4 farm cases were selected. Each farm case comprised of 70 serum samples which had been maintained at -20°C for about 24 months. The 70 samples were collected from 10 weaned piglets, 10 nursery pigs, 10 grower pigs, 10 finisher pigs, 10 breeding gilts and 20 sows. One additional case of 60 samples was also selected which comprised of 30 sera from nursery pigs, evenly distributed among 1 week, 4 weeks and 7 weeks post-weaning, 10 breeding gilts and 20 sows. PCV-2 antibody was measured in each of the 340 samples, using techniques previously described (Ellis, 1999, Walker, in press).

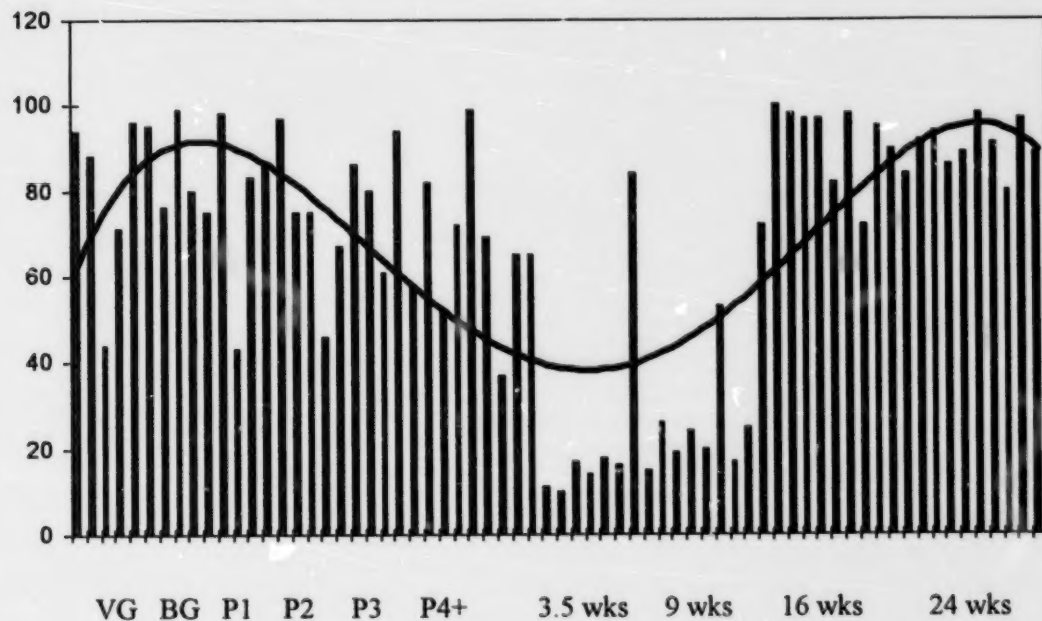
#### **Results**

Antibodies to PCV-2 were detected in all herds and followed a consistent pattern (Figure 1). The highest and most consistent antibody titres were noted in the grower and finisher populations. The lowest antibody titres were noted in the suckling and nursery pigs (Table 1). Antibody titres in the sow herd were consistently positive, but lower and more variable than the grower and finisher pigs.

#### **Conclusion:**

The pattern of antibody production and decay was similar to other swine diseases. Low titres were detected in the suckling and were presumed to originate from the consumption of colostrum (maternal antibody) at birth. After weaning, nursery pigs were exposed and rapidly produced antibody to PCV-2. All herds tested were infected with PCV-2, with active viral circulation resulting in the continued cycling of virus in young pigs. Because all grower and finisher pigs were exposed to the virus, it is hypothesized that PCV-2 is rapidly spread from pig to pig in affected farms. Sow herds were the least reliable age group to test. It was determined that future serologic testing would be performed in pigs ranging in age from weaning to market. Ten samples per age group would be sufficient to detect PCV-2 on infected farms.

**Figure 1.** Typical PCV-2 antibodies detected using the competitive ELISA in infected herds.



Bars represent the antibodies of individual pigs tested at various ages: VG-virgin gilts, BG-bred gilts, P1-parity 1 sows, P2-parity 2 sows, P3-parity 3 sows, P4+-parity 4 and older sows. The solid line represents the average titre for all animals in each age group.

**Table 1. PCV-2 antibody characteristics by age group.**

| Age Group     | No of Samples | Mean (S.D.) Titre        | Percent Positive  | Titre Variability (CV) |
|---------------|---------------|--------------------------|-------------------|------------------------|
| Sow herd      | 138           | 68.6 (25.6) <sup>a</sup> | 92.8 <sup>d</sup> | 37.4                   |
| Suckling pigs | 56            | 58.2 (31.6) <sup>b</sup> | 78.6 <sup>c</sup> | 54.3                   |
| Nursery pigs  | 46            | 52.9 (36.6) <sup>b</sup> | 63.0 <sup>c</sup> | 69.2                   |
| Grower pigs   | 40            | 93.1 (7.9) <sup>c</sup>  | 100 <sup>d</sup>  | 8.5                    |
| Finisher pigs | 40            | 92.0 (10.3) <sup>c</sup> | 100 <sup>d</sup>  | 11.2                   |

Values within columns with differing superscripts are statistically different,  $p < 0.05$

## **Experiment 2:**

### **Investigating the sero-epidemiology of porcine circovirus type-2 infection in breeding stock herds**

#### **Introduction**

Genex Swine Group is a premier supplier of breeding stock to the Canadian market place, with approximately 40 herds producing breeding stock in Canada. Within these herds, PMWS has been evident for several years, but only in a select number of herds. In affected herds, clinical signs have been sporadic. Thus, the Genex system provided an excellent opportunity to study the distribution of PCV-2 within related herds of a large production system. The objective of this study was to investigate the epidemiology of PCV-2, in relationship to the clinical presentation, antibody production, post-weaning mortality, facility type and source herd.

#### **Specific Objectives**

1. To determine patterns of antibody development and decay by age group in clinically affected and clinically unaffected herds.
2. Examine the Genex system to detect potential differences in antibody levels by production or unit type (farrow to finish, multi-site), health status, and pyramid.
3. To investigate potential associations between antibody titre and post-weaning mortality rate, and clinical signs.

#### **Materials and Methods**

Support was solicited from approximately 40 Genex production nucleus and multiplication herds, representing about equal numbers of herds experiencing or not experiencing clinical PMWS. All were Canadian herds located in Quebec, Ontario, Manitoba, Saskatchewan, Alberta and British Columbia. They were sourced by one of two genetic nuclei located in Saskatchewan. The health status of each herd was monitored monthly by the herd veterinarian and all herds were required to report the clinical health status to Genex on a monthly basis.

Sampling was undertaken by the herd veterinarian, or designated personnel under his/her supervision. From each herd 10 pigs (40 total) were bled from each of the following age groups:

- weaned or unweaned piglets at 21 - 24 days of age
- nursery pigs at 25 - 28 kgs
- grower pigs at 60 - 63 kgs
- finisher pigs 95 - 100 kgs.

Five to six milliliters (mL) of blood were harvested in a serum tube which yielded a minimum 2 mL serum. Sampling was randomly distributed across all rooms/pens containing pigs of the age

group specified. All pigs sampled were clinically healthy and not exhibiting signs of PMWS. Serum was submitted and analysed for PCV-2 antibody levels at the University of Saskatchewan, using the competitive ELISA. Samples with % inhibition above 25% were considered positive. During the farm visit, the veterinarian and producer completed a brief epidemiologic survey which was used to gather general farm information, productivity data, a score by age group for various clinical signs commonly noted on swine farms, and diagnostic information related to PMWS if it had been diagnosed on the farm. Clinical scores were assigned as 0-3 (0=absent, 1=uncommon, 2=common, 3=very common) based on the veterinarian's clinical impression of the herd at the time blood samples were drawn. All statistical analysis was performed using commercial software Statistics v4.0.

### Results:

Serum samples and a completed survey was received from 26 herds. Of these, one herd was excluded from the study because samples were not received from all age groups. Of the remaining 25 herds, 13 had not experienced clinical disease resembling PMWS (PMWS negative), 12 had experienced clinical disease (PMWS positive), and 1 herd had an unknown status. There were no differences in the mean, prevalence or variability of PCV-2 antibody levels in the PMWS positive herds compared to the PMWS negative. Across all herds, the mean titre and positive sero-prevalence (% animals with positive tests) was significantly higher in the finisher, than the other age groups. In addition the titre variability (a measure of virus activity and sero-conversion) was significantly lower in the finishers compared to the other age groups (Table 2).

Herds exhibiting clinical PMWS were significantly larger and suffered higher post-weaning mortality than herds without clinical disease. Furthermore, clinical herds reported more pale and jaundice pigs compared to non-clinical herds and the overall clinical score for the nursery area were higher for clinical herds reflecting significantly higher numbers of sick pigs (Table 3). The association between PCV-2 titres and specific clinical scores for coughing, dyspnea (breathing difficulty), rough hair coat, pallor, unthriftiness in the nursery were low but bordered on statistical significance in *Mycoplasma hyopneumoniae* negative herds.

Clinical signs were associated with antibody titre level in some age groups. Low titres in nursery pigs were associated with more clinical signs in grower pigs ( $r = -0.39$ ,  $p = 0.05$ ). In addition, herds with a high clinical scores had more variable titres particularly in the grower and finisher ( $r = 0.41$ ;  $p = 0.04$  for grower,  $r = 0.38$ ;  $p = 0.05$  for finisher). There were no statistical differences in antibody level between unit type, pyramid or source herd and unit type.

### Discussion & Conclusions:

PMWS positive herds experience post-wean mortality rates on average two fold higher than negative herds. This is significant by itself, but particularly in the light of recent research suggesting that clinical PMWS is a multi-factorial disease, made worse by multiple infection (Allan et al, 2000, Harmes et al, 2000). However, no significant differences in PCV-2 antibody

titre levels were detected in clinical (PMWS positive) versus non-clinical (PMWS negative) herds, which further supports the hypothesis that clinical expression is enhanced by other factors including multiple infections. Antibody titres were evident in all herds. PCV-2 serology is a useful tool to determine the presence or absence of the virus in the herd, or to determine the age group in which pigs are exposed. When present, PCV-2 exhibits such high prevalence that only a small number of samples need to be drawn. Furthermore, bleeding should be performed in grower or finisher pigs.

On farm control strategies should be targeted at controlling concurrent diseases affecting weaned pigs, particularly in the nursery and grower age groups. Antibiotics are ineffective for PCV-2 alone, but useful for the control of other bacterial diseases. Field experiences have shown that minimizing stress and controlling the environment are important factors for reducing clinical disease on affected farms.

Recent studies (Garveau, 1999, Ohlinger, 2000-person communication) have suggested a very high likelihood intra-uterine infection. Moreover, this may help to propagate PCV-2 infection in the herd and facilitate immune-tolerance and the clinical expression of PMWS. As such, pre-colostrum sampling of neonatal piglets may be the most useful method of evaluating the possibility of intra-uterine vertical transmission and sow herd virus circulation. This may also help elucidate the significance of the high titre variability in the suckling and nursery age groups.

In the Genex system, PCV-2 titres are associated with clinical disease in the nursery, particularly for coughing, pallor, rough hair coat and unthriftiness. More importantly, PCV-2 infection exists in all herds tested to date, regardless of PMWS status, and that PCV-2 is actively circulating in young piglets in all herds, resulting in 100% exposure of pigs. Absence of clinical signs does not imply absence of PCV-2. Thus, serology is the only definitive method of determining PCV-2 status, and health monitoring procedures of breeding stock suppliers should reflect this. However, purchasing breeding stock from PCV-2 negative farms does not appear to be possible or necessary for controlling clinical disease.

Future research should clearly be focused on understanding the disease pathogenesis, ie what factors are necessary for the development of clinical disease. PMWS is not caused solely by PCV-2, but by PCV-2 in combination with other factors. Elucidating these factors is essential for long term control in the industry. The significance of in-utero infection (infection during pregnancy) on clinical expression and reproductive performance should also be clarified. Furthermore, the effect of PCV-2 on boar fertility, semen quality and the subsequent fertility of artificially inseminated females is a priority for future research and currently a significant concern for the semen production centers in the country.

Table 2. PCV-2 antibody levels by age group across all farms

| Age Group     | Mean (S.D.)<br>Titre     | Percent<br>Positive      | Titre Variability<br>(CV) |
|---------------|--------------------------|--------------------------|---------------------------|
| Suckling pigs | 64.0 (16.4) <sup>b</sup> | 78.2 (19.6) <sup>b</sup> | 46.1 (22.9) <sup>b</sup>  |
| Nursery pigs  | 34.4 (13.5) <sup>c</sup> | 45.6 (21.3) <sup>c</sup> | 66.1 (8.5) <sup>c</sup>   |
| Grower pigs   | 70.9 (23.1) <sup>b</sup> | 82.9 (22.7) <sup>b</sup> | 31.6 (29.6) <sup>b</sup>  |
| Finisher pigs | 91.7 (8.3) <sup>a</sup>  | 98.8 (4.4) <sup>a</sup>  | 11.3 (11.1) <sup>a</sup>  |

Values within columns with differing superscripts are statistically different,  $p < 0.001$

Table 3. Comparison of clinical and non-clinical herds

| Variable                  | Clinical<br>PMWS Positive | Non-clinical<br>PMWS Negative | Significance |
|---------------------------|---------------------------|-------------------------------|--------------|
| Herd size (# sows)        | 947                       | 502                           | $p = 0.05$   |
| Post-wean mortality rate  | 4.5                       | 2.4                           | $p = 0.06$   |
| Clinical score - jaundice | 1.2                       | 0.0                           | $p = 0.01$   |
| Clinical score - pallor   | 2.7                       | 1.0                           | $p = 0.001$  |
| Overall clinical score    | 9.9                       | 5.6                           | $p = 0.002$  |

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## Postweaning multisystemic wasting syndrome: Epidemiology and clinical presentation

John C. S. Harding, DVM, MSc; Edward (Ted) G. Clark, DVM, MVSc; John H. Strokappe, DVM; Phil I. Willson, DVM, PhD; John A. Ellis, DVM, PhD

### Summary

**Objective:** To describe the characteristics of postweaning multisystemic wasting syndrome (PMWS).

**Methods:** A retrospective analysis of the production records of a 600-sow herd with clinical signs consistent with endemic PMWS was conducted. Also, data elicited by a descriptive epidemiologic survey that was completed by 15 producers with herds that had confirmed PMWS was analyzed.

**Results:** In the case herd, postweaning mortality rate peaked at 7.67% on month 9 of the epidemic, then returned within 16 months to pre-outbreak levels of 2.1%–2.5%. The most common causes of death reported by the farm were unthriftiness (weight loss, emaciation), jaundice (liver disease), and dyspnea (respiratory disease). In the surveyed herds, PMWS was found to be a slow and progressive disease with a high case fatality rate (81.4%  $\pm$  23.4%). Clinical disease was observed most commonly in pregrower barns (90%), followed by nursery (62%) and grower barns (39%). The syndrome was first noted in pigs 42  $\pm$  13.5 days of age. The most frequent clinical signs of PMWS included unthriftiness, dyspnea, pallor, rough hair coat, diarrhea, and jaundice. Postweaning mortality averaged 6.7%  $\pm$  5.1% (SD) in affected herds, and was reported as 18.3% in the most severely affected herd. Poor response to various modes of antimicrobial therapy was reported.

**Implications:** Control of PMWS is difficult and may depend largely on pig flow, improved sanitation, and early recognition and segregation of sick pigs.

**Keywords:** swine, porcine circovirus, postweaning multisystemic wasting syndrome

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In January 1995, a 600-sow farrow-to-finish swine operation reported high mortality in pigs 3–8 weeks postweaning. Affected pigs demonstrated severe weight loss, tachypnea, dyspnea, pallor, enlarged lymph

nodes, and/or jaundice. The disease was described as subtle and progressive, with high mortality in affected pigs. Various antimicrobial agents were tried, but response was poor and most affected pigs died or were euthanized after 3–4 weeks of illness. After an exhaustive diagnostic work-up, pathologists failed to identify any etiologic agent, but successfully ruled out all bacterial pathogens common to swine. The disease was named postweaning multisystemic wasting syndrome (PMWS), based on its unique clinical presentation and histopathologic lesions.<sup>1–3</sup>

Porcine circovirus (PCV) has been suspected of an etiologic role in PMWS after investigators identified deeply basophilic staining intracytoplasmic inclusion bodies that contained clusters of PCV.<sup>4</sup> Evidence for a possible association was strengthened by the isolation of PCV from tissues of PMWS-affected pigs<sup>5</sup> and from positive immunohistochemical staining of PCV antigen in affected tissues.<sup>2</sup> At the time of writing, Koch's postulates have not yet been fulfilled, but inoculation studies with cloned virus are underway.

Porcine circovirus (PCV) was first identified as a noncytopathic contaminant of continuous PK-15 cell line.<sup>6</sup> Although other members of the Circoviridae family are pathogenic (psittacine beak and feather disease, chicken anaemia virus), until recently porcine circovirus had not been clearly associated with disease in pigs or other species.<sup>7–9</sup> Because serum antibodies to PK-15 circovirus are widespread in the swine industries of Germany,<sup>9</sup> Canada,<sup>10</sup> England,<sup>11</sup> and the United States,<sup>12</sup> the true involvement of PCV in PMWS is not fully understood, but is hypothesized to involve a variant strain.<sup>5</sup>

Because the unique histopathologic lesions characteristic of PMWS have been previously described,<sup>2,13</sup> the objective of this paper is to present descriptive epidemiologic data from epidemically and endemically affected herds.

### Materials and methods

#### Case herd

A retrospective analysis of production data was undertaken from the 600-sow farrow-to-finish herd that experienced severe mortality in 1995 due to PMWS. Production data from January 1994–December 1996 were analyzed, including data from 10 months of baseline production before the first signs of PMWS were reported, and 10 months production data after PMWS had subsided. Percent postweaning mortality over a rolling 3-month period was available from computerized production records (Easicare Systems Inc., Fyfieldwick, United Kingdom).

JCSH: Harding Swine Veterinary Service, Inc, P.O. Box 2922, Humboldt, Saskatchewan, S0K 2A0, Canada; EGC, JAE: Western College of Veterinary Medicine; JHS: Parkland Veterinary Service; PIW: Veterinary Infectious Disease Organization

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A more detailed description of mortality was available from production records maintained by barn staff on a daily basis. Pertinent information from every pig that died on the unit was recorded, including the date of death, tattoo number, room location, stage of production, and cause of death or description of clinical signs immediately prior to death. For the purpose of this study, the case definition of PMWS included deaths associated with "unthriftiness," "jaundice," "respiratory distress (puffer or dyspnea)," and "unknown reasons." The latter was included because early in the epidemic, it was the category used to record most deaths associated with "unthriftiness."

During the PMWS outbreak, the clinical course was monitored daily by barn staff and herd veterinarians. To rule out porcine reproductive and reproductive syndrome virus (PRRSV), antibody testing was undertaken on two occasions during the outbreak. In January 1995, 80 blood samples were collected from 15 suckling pigs (5 kg, 11 lb), 15 nursery pigs (15 kg, 33 lb), 15 grower pigs (50 kg, 110 lb), 15 finisher pigs (100 kg, 220.5 lb), 10 replacement females (120 kg, 264.5 lb), and 10 mature sows. Serum was harvested and analysed for PRRSV IgG antibody using the indirect-immunofluorescent antibody (IFA) test for the Lelystad and ATCC VR-2332 strains.<sup>14</sup> In May 1995, sera was harvested from thirty 50-kg (110-lb) pigs and was analysed for PRRSV IgG antibody using the IDEXX ELISA.<sup>15</sup>

## Epidemiologic survey

By late 1996, numerous Western Canadian swine herds were experiencing clinical disease consistent with PMWS. To gather descriptive epidemiologic data on affected farms, a standardized survey was distributed to affected herds via their attending herd veterinarian. Only herds with a confirmed positive diagnosis of PMWS based on histopathologic examination from multiple pigs and tissues were included in the survey. To maintain consistency, all histopathologic examinations were performed by Dr. Ted Clark, Western College of Veterinary Medicine, Saskatoon, Canada.

The epidemiologic data collected on the survey were subdivided into four sections as follows:

- general farm information and location,
- herd productivity,

- health status of unit, and
- PMWS clinical description.

The health status of each herd was assessed by the attending veterinarian based on their farm visits and veterinary consultations, available diagnostic reports originating from necropsy examinations, serology, slaughter checks examinations, and from health documentation of the source herd(s) provided by the seedstock supplier.

Descriptive statistics were performed using commercial software (Statistix version 4.0, Analytical Software, Tallahassee, Florida).

## Results

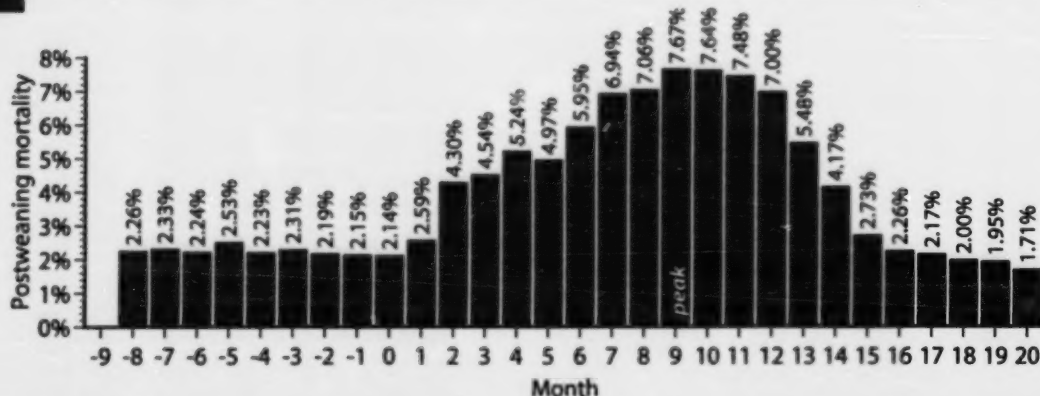
### Case herd

The clinical outbreak lasted from December 1994–March 1996. Clinically diseased pigs were most frequently noted in the nursery and grower stages, and were rarely noted before weaning. Postweaning multisystemic wasting syndrome was first observed in pigs at 6–8 weeks of age (3–5 weeks postweaning). Initial clinical signs were a subtle weight loss and increased weight variation among pen groups. Although the course of the disease was protracted, the onset of clinical signs in affected pigs was very often unnoticeable in the early stages. Postweaning mortality increased for 16 months, beginning in December 1995, and peaked in month 9 at 7.67% compared to the pre-outbreak postweaning mortality rate of 2.1%–2.5% (Figure 1). The most frequent clinical signs prior to death were unthriftiness, dyspnea, and jaundice (Figure 2), compared to the other clinical signs including lameness, heart failure, arthritis, diarrhea, intestinal torsion, pallor, sudden death, and stress/fighting. Postweaning multisystemic wasting syndrome accounted for 76% of the mortality in the nursery stage and 43% of the mortality in the grower-finisher stage. All serologic samples were negative by IFA and ELISA for the PRRSV antibody for VR-2332 and the Lelystad strains.

### Epidemiologic survey

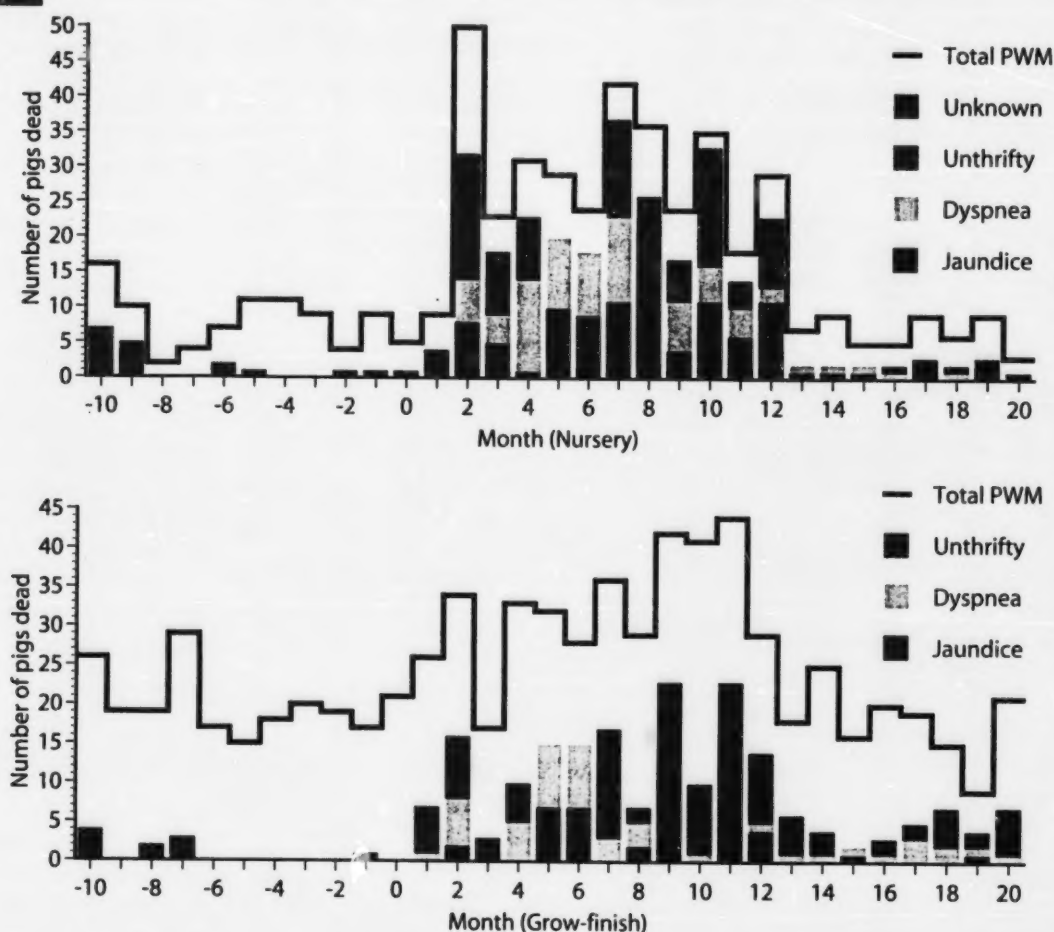
Surveys were completed by 60% of the farms contacted (15 farms). All herds from which a response was received were in Saskatchewan and Alberta. All herds surveyed were farrow-to-finish herds with 80–500

Figure 1



Changes in total postweaning mortality (%) in the case herd during the acute or epidemic presentation of PMWS

Figure 2



Proportion of postweaning mortality associated with PMWS compared to total mortality in the nursery (upper graph) and grow-finish (lower graph) stages during the epidemic presentation in a single herd  
Distance between total line and top of bars indicates non-PMWS-related mortality.

sows. All herds had continuous-flow grower and finisher barns, 53% had continuous-flow nurseries, and 60% had continuous-flow farrowing rooms. The age of the herds ranged from 1–25 years in operation since inception or depopulation, but 60% were less than 5 years old. All herds were situated at least 0.8 km (0.5 miles) from the neighboring hog operation, and 50% were > 2.4 km (1.5 miles). Performance (mean  $\pm$  standard deviation) on farms was good to excellent:

- litters per sow per year:  $2.3 \pm 0.2$ ;
- liveborn litter size:  $10.7 \pm 0.6$ ;
- preweaning mortality:  $11.4\% \pm 4.4$ ; and
- weaned per litter:  $9.3 \pm 0.6$ .

All of the herds were clinically free of *Actinobacillus pleuropneumoniae*, swine dysentery, and transmissible gastroenteritis, and most were also clinically free of *Mycoplasma hyopneumoniae* pneumonia (Figure 3). The diseases or pathogenic agents that were endemic to most herds included PRRSV, ileitis associated with *Lawsonia*

*intracellularis*, and *Haemophilus parasuis* (Figure 3).

The effects of PMWS were longstanding in some of the herds, averaging 18 months among the surveyed herds. Pigs with PMWS developed initial clinical signs at  $42 \pm 13.5$  days of age. Clinical disease was noted most commonly in the nursery and the pregrower stages of production (Figure 4). The most frequent clinical signs reported were unthriftiness, dyspnea, pallor, rough hair coat, jaundice, and diarrhea (Figure 5). The postweaning mortality rate was  $6.7\% \pm 5.1\%$  and the subjective case fatality rate of PMWS affected pigs was  $81.4\% \pm 23.4\%$ . Poor response to various modes of antimicrobial therapy was reported on all farms.

## Discussion

Postweaning multisystemic wasting syndrome is a new and unique disease affecting swine. It results in significant nursery and grow-finish mortality, and is characterized by unthriftiness, dyspnea, rough hair

A more detailed description of mortality was available from production records maintained by barn staff on a daily basis. Pertinent information from every pig that died on the unit was recorded, including the date of death, tattoo number, room location, stage of production, and cause of death or description of clinical signs immediately prior to death. For the purpose of this study, the case definition of PMWS included deaths associated with "unthriftiness," "jaundice," "respiratory distress (puffer or dyspnea)," and "unknown reasons." The latter was included because early in the epidemic, it was the category used to record most deaths associated with "unthriftiness."

During the PMWS outbreak, the clinical course was monitored daily by barn staff and herd veterinarians. To rule out porcine reproductive and reproductive syndrome virus (PRRSV), antibody testing was undertaken on two occasions during the outbreak. In January 1995, 80 blood samples were collected from 15 suckling pigs (5 kg, 11 lb), 15 nursery pigs (15 kg, 33 lb), 15 grower pigs (50 kg, 110 lb), 15 finisher pigs (100 kg, 220.5 lb), 10 replacement females (120 kg, 264.5 lb), and 10 mature sows. Serum was harvested and analysed for PRRSV IgG antibody using the indirect-immunofluorescent antibody (IFA) test for the Lelystad and ATCC VR-2332 strains.<sup>14</sup> In May 1995, sera was harvested from thirty 50-kg (110-lb) pigs and was analysed for PRRSV IgG antibody using the IDEXX ELISA.<sup>15</sup>

## Epidemiologic survey

By late 1996, numerous Western Canadian swine herds were experiencing clinical disease consistent with PMWS. To gather descriptive epidemiologic data on affected farms, a standardized survey was distributed to affected herds via their attending herd veterinarian. Only herds with a confirmed positive diagnosis of PMWS based on histopathologic examination from multiple pigs and tissues were included in the survey. To maintain consistency, all histopathologic examinations were performed by Dr. Ted Clark, Western College of Veterinary Medicine, Saskatoon, Canada.

The epidemiologic data collected on the survey were subdivided into four sections as follows:

- general farm information and location,
- herd productivity,

- health status of unit, and
- PMWS clinical description.

The health status of each herd was assessed by the attending veterinarian based on their farm visits and veterinary consultations, available diagnostic reports originating from necropsy examinations, serology, slaughter checks examinations, and from health documentation of the source herd(s) provided by the seedstock supplier.

Descriptive statistics were performed using commercial software (Statistix version 4.0, Analytical Software, Tallahassee, Florida).

## Results

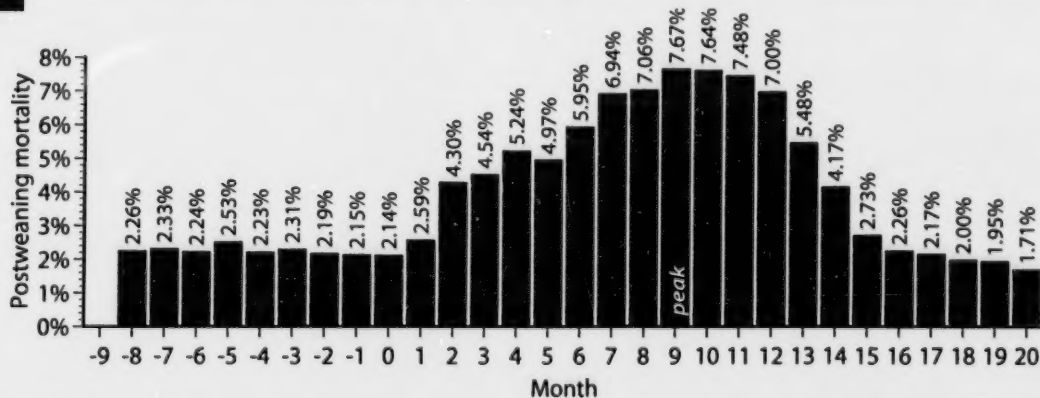
### Case herd

The clinical outbreak lasted from December 1994–March 1996. Clinically diseased pigs were most frequently noted in the nursery and grower stages, and were rarely noted before weaning. Postweaning multisystemic wasting syndrome was first observed in pigs at 6–8 weeks of age (3–5 weeks postweaning). Initial clinical signs were a subtle weight loss and increased weight variation among pen groups. Although the course of the disease was protracted, the onset of clinical signs in affected pigs was very often unnoticeable in the early stages. Postweaning mortality increased for 16 months, beginning in December 1995, and peaked in month 9 at 7.67% compared to the pre-outbreak postweaning mortality rate of 2.1%–2.5% (Figure 1). The most frequent clinical signs prior to death were unthriftiness, dyspnea, and jaundice (Figure 2), compared to the other clinical signs including lameness, heart failure, arthritis, diarrhea, intestinal torsion, pallor, sudden death, and stress/fighting. Postweaning multisystemic wasting syndrome accounted for 76% of the mortality in the nursery stage and 43% of the mortality in the grower-finisher stage. All serologic samples were negative by IFA and ELISA for the PRRSV antibody for VR-2332 and the Lelystad strains.

### Epidemiologic survey

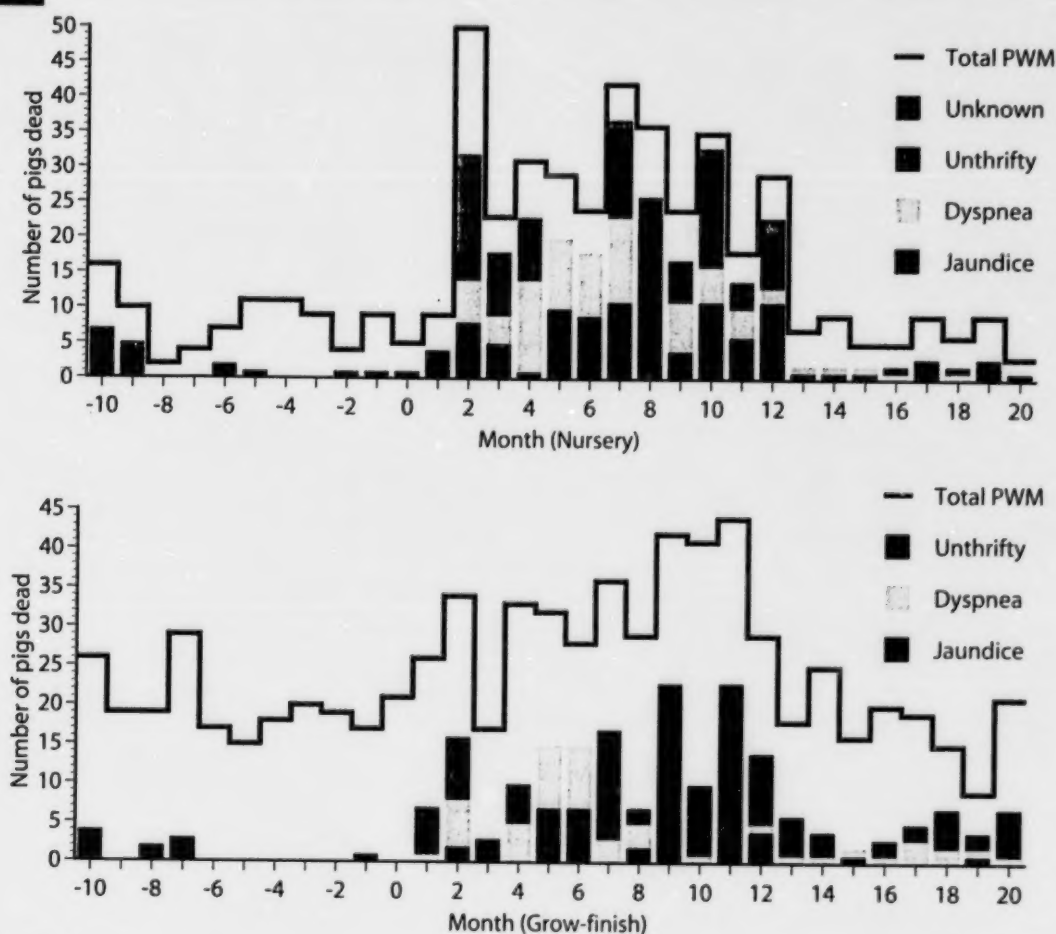
Surveys were completed by 60% of the farms contacted (15 farms). All herds from which a response was received were in Saskatchewan and Alberta. All herds surveyed were farrow-to-finish herds with 80–500

Figure 1



Changes in total postweaning mortality (%) in the case herd during the acute or epidemic presentation of PMWS

Figure 2



Proportion of postweaning mortality associated with PMWS compared to total mortality in the nursery (upper graph) and grow-finish (lower graph) stages during the epidemic presentation in a single herd  
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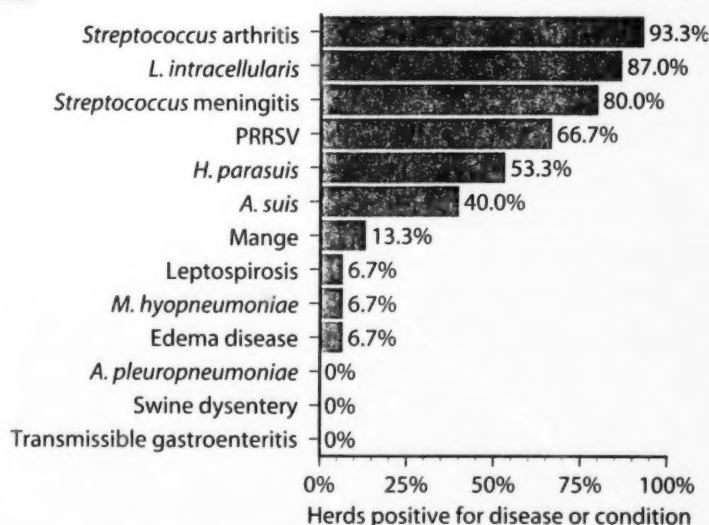
coat, pallor, jaundice, and diarrhea, and (less frequently) coughing and central nervous system disturbances. The most frequent necropsy lesions are systemic lymphadenopathy, interstitial pneumonia, hepatocellular apoptosis, lymphohistiocytic infiltration of gastric, cecal and colonic mucosa, splenic B-cell follicles loss, infiltration of T cell areas by histiocytic cells, and deeply basophilic stained clusters of intracytoplasmic inclusion bodies in B-cell-dependent areas of lymphatic tissue.<sup>2,13</sup>

Since the outbreak subsided in the case herd, pre-outbreak levels of performance (1.95% postweaning mortality) have been achieved and maintained for 18 months, although sporadic cases of PMWS have been noted. Although there is no definitive reason why mortality returned to pre-outbreak levels, we hypothesize that implementing strict all-in-all-out pig flow, improving washing and disinfection techniques, and segregating and euthanizing pigs in a more timely fashion reduced infection pressure and viral transmission to susceptible pigs. Natural immunity to the causative agent is presumed to have developed during the course of the outbreak, thus reducing the risk of transplacental infection, viremia, exposure to high concentrations of the causative agent, and failure to transfer passive antibodies.

Although a limited number of herds were included in the survey, the epidemiologic data reported is the first available on the effects of endemic PMWS. Many of those herds that did not respond to the survey had experienced PMWS for less than 3 months and therefore had only a partial understanding of the effect of PMWS on their herd productivity. Affected pigs in this survey consistently developed clinical disease around 42 days of age; however, more recent field experience suggests that the age of first onset may be associated with pig flow, the degree of facility compartmentalization, and the ability of the management to segregate and remove affected pigs.<sup>16</sup> High concentrations of maternal antibody may also provide a protective effect, hence delaying the onset of clinical signs.

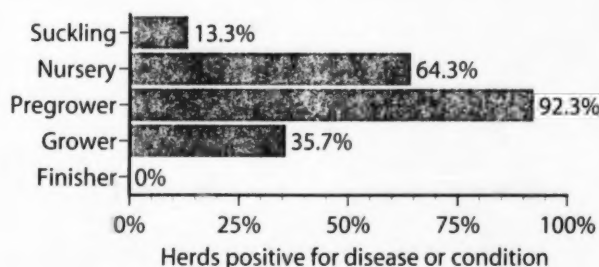
There is evidence to suggest that PMWS is associated with infection with porcine circovirus, although a causal relationship has not yet been confirmed. The putative association is supported by the positive immunohistochemical staining of virtually all affected tissues, EM identification of inclusion bodies characteristic of porcine circovirus, and the isolation of PCV from affected pigs.<sup>5</sup> The predilection of porcine circovirus for macrophages, monocytes, histiocytes, and antigen-presenting macrophages in lung, thymus, and spleen suggests that PCV

**Figure 3**



Health status of herds included in the epidemiologic survey

**Figure 4**



Proportion of the surveyed herds that noted PMWS in suckling, nursery, pregrower, grower, and finisher pigs

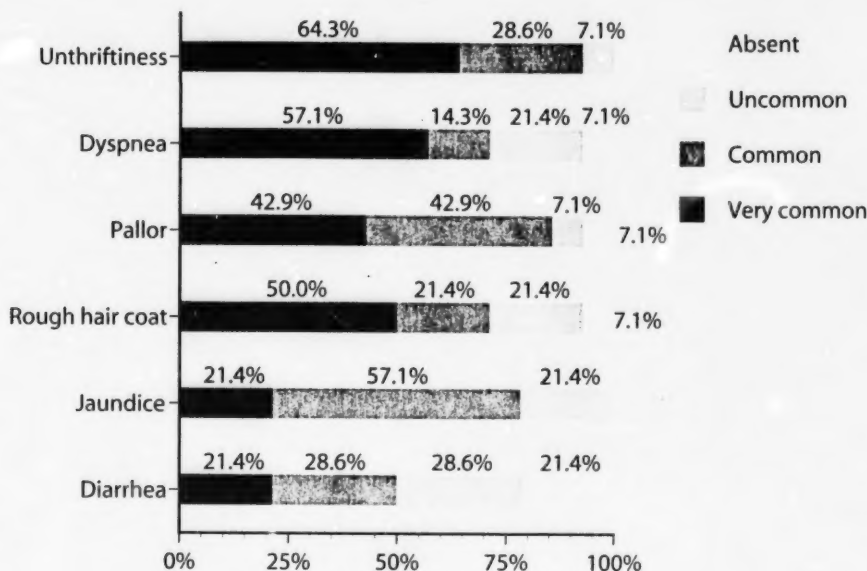
pathogenesis may be the result of immune dysfunction. Immunosuppressive effects are common to other members of the Circoviridae family.<sup>17</sup>

Interactions with other viruses in the pathogenesis of PMWS have not been ruled out. However, PMWS is an entity entirely distinct from PRRSV and can be clinically devastating in herds that are clinically and serologically free of United States and European PRRSV strains based on repeated PRRSV IgG testing. The two diseases can be differentiated both clinically and pathologically:

- the presence of icterus and gross and histologic liver lesions in affected pigs are characteristic of PMWS but not PRRS;
- histologic lesions in lymph tissue are characterized by depletion in cases of PMWS, whereas proliferation is the characteristic lesion in cases of PRRS;
- gross and histologic kidney and liver lesions are noted frequently with PMWS but are not noted in PRRS.

Recently, a novel virus similar to the human hepatitis E virus was

Figure 5



Relative frequency of the 6 most common clinical sign of PMWS in surveyed herds

identified as a cause of multifocal lymphoplasmacytic and necrotizing hepatitis with random hepatocellular swelling and vacuolation.<sup>18</sup> Although similar in nature, the association between swine hepatitis E and PMWS is not fully understood.

Studies on the etiology of PMWS are ongoing at the time of this writing. There is strong immunohistochemical evidence of PCV antigen in lesional tissue, but experimental transmission studies using purified virus must be completed. Although antibodies to porcine circovirus are widespread in the pig industry,<sup>9-12</sup> these studies only confirm the presence of PK-15 strain PCV antibody. The strain of PCV putatively associated with PMWS is unique<sup>5</sup> and no industry-wide serologic testing has been performed with the strain of PCV associated with disease. Thus, the mutation of a nonpathogenic PK-15 strain PCV to a more virulent strain remains a possibility.

It is unfortunate that more is not known about the epidemiology of the syndrome at present. However, further epidemiologic studies including a serologic case-control investigation will be undertaken as soon as the etiologic agent has been identified and a sensitive, specific antibody test is available. In addition, studies are planned that will more clearly elucidate the pattern of transmission on affected farms, identify any potential risk factors for susceptible pigs, and determine the relative frequency of clinical signs and performance in affected and non-affected pigs within the same cohort.

## Implications

- Practicing veterinarians should be aware that PMWS involves postweaning wasting or unthriftiness and should be considered particularly where jaundice is noted, or in PRRS-free herds where dys-

pnea is noted.

- Postweaning multisystemic wasting disease most commonly affects nursery pigs around 42 days of age ( $\pm 2$  weeks).
- The severity and duration of the syndrome varies from herd to herd; clearly, more research is needed to identify potential risk factors associated the clinical presentation and epidemiology of the syndrome.

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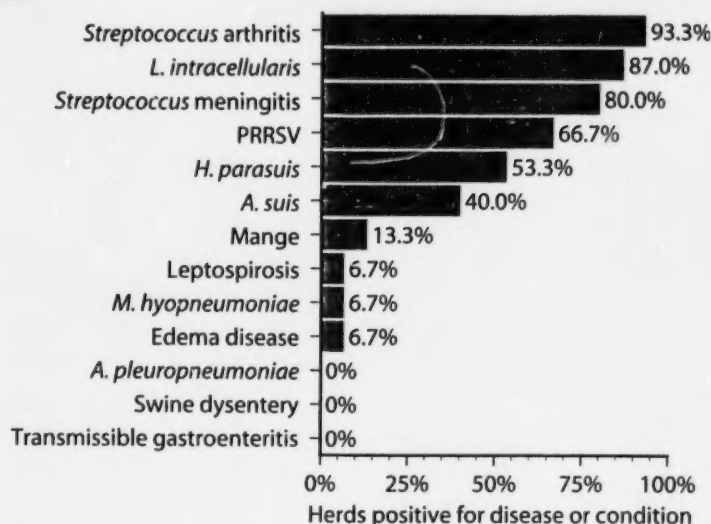
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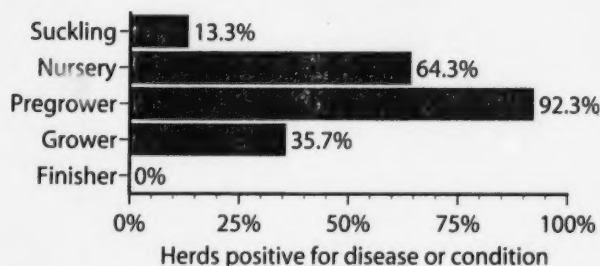
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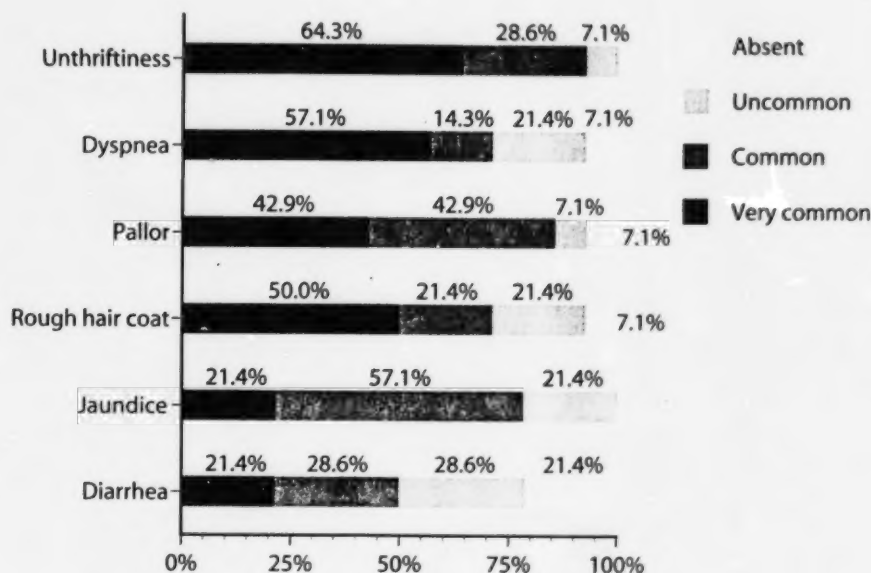
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